CELL BIOLOGY

Intercellular communication in the kidney

ECVs could be used as vehicles to deliver RNA therapies to target cells in the kidney

Vasopressin selectively regulates the uptake of extracellular vesicles (ECVs) in the renal collecting duct, say researchers. Based on their new findings, James Dear and colleagues suggest that ECV transfer is a mechanism of intercellular communication that could potentially be utilized for targeted drug delivery.

“ECVs are tiny particles that contain proteins and RNA from their cell of origin,” explains Dear. “They are present in urine and have been

demonstrated to transfer signals between cells, at least *in vitro*. Our question was whether the uptake of ECVs by kidney tubular cells is a regulated process.”

The researchers previously found that vasopressin regulates the aquaporin 2 content of ECVs. Now, they report that the vasopressin analogue desmopressin stimulated a murine collecting duct cell line (mCCD_{cl1}) to take up ECVs derived from kidney tubule cells, but not those derived from juxtaglomerular cells. Treatment with tolvaptan — a vasopressin V2 receptor antagonist — abrogated desmopressin-induced ECV uptake. Moreover, desmopressin-stimulated mCCD_{cl1} cells downregulated miRNA-503 target genes in response to incubation with miRNA-503-loaded ECVs, but no significant change in gene expression occurred in the absence of desmopressin.

To investigate the effect of vasopressin on renal uptake and urinary excretion of ECVs *in vivo*, Dear and colleagues intravenously injected mice with fluorescently loaded ECVs derived from mCCD_{cl1} cells. They found that tolvaptan treatment

induced a fivefold increase in fluorescent ECVs in the urine of these mice, together with a reduction in ECV deposition in renal tissue. By contrast, in a patient with central diabetes insipidus — a condition that results from vasopressin deficiency — intranasal administration of desmopressin reduced the urinary excretion of ECVs derived from glomerular and proximal tubule cells. The researchers note that these findings are consistent with vasopressin-regulated uptake of glomerular and proximal tubule ECVs by the distal segments of the nephron.

“The uptake of ECVs into kidney collecting duct cells is tightly regulated by vasopressin *in vitro* and *in vivo*,” concludes Dear. “This system can be manipulated using drugs that are already approved for clinical use.” The researchers also suggest that ECVs could be used as vehicles to deliver RNA therapies to target cells in the kidney.

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